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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/963,340	09/24/2001	Mark A. Conkling	5051.338CT	1188

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EXAMINER	
KALLIS, RUSSELL	

ART UNIT	PAPER NUMBER
1638	

MAIL DATE	DELIVERY MODE
10/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/963,340	CONKLING ET AL.	
	Examiner	Art Unit	
	Russell Kallis	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,12,13,16-19,26,31-33,43-45,57,61,62,95-100 and 103-107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,12,13,16-19,26,31-33,43-45,57,61,62,95-100 and 103-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/20/2007 has been entered.

Rejection of Claims 1-3, 12-13, 16-19, 26, 31, 43-45, 57 and 94-107 under the judicially created doctrine of obviousness-type double patenting is withdrawn in view of Applicant's submission of a terminal disclaimer.

Rejection of Claims 26 and 43-45 under 35 U.S.C. 101, is withdrawn in view of Applicant's amendments.

Claims 94-107 are new. Claims 1-3, 12-13, 16-19, 26, 31-33, 43-45, 57, 61, 62, 95-100, and 103-107 are pending and examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

Claims 26 and 43-45 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. See MPEP § 608.01(n).

A series of singular dependent claims is permissible in which a dependent claim refers to a preceding claim which, in turn, refers to another preceding claim.

A claim which depends from a dependent claim should not be separated by any claim which does not also depend from said dependent claim. It should be kept in mind that a dependent claim may refer to any preceding independent claim. In general, applicant's sequence will not be changed. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 112

Claims 1-3, 12-13, 16-19, 26, 31-33, 43-45, 57, 61-62, 95-100 and 103-107 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection. This rejection is maintained for the reasons of record set forth in the Official action mailed 7/19/2006. Applicant's arguments filed 8/20/2007 have been considered but are not deemed persuasive.

Applicant asserts that the amendments to the claims have overcome the NEW MATTER rejection and recite portions of the specification that provide support (response page 7-8). The current claims (especially claims 1 and 95-100) are drawn to antisense fragments (i.e. an isolated nucleic acid that hybridizes to tobacco QPRtase mRNA) and there is support in the specification for antisense species recited in the claims of at least 30, 50, 75, 100, 125, 150 or 200 consecutive (i.e. contiguous) nucleotides, wherein the fragment is complementary to the mRNA. However, those fragments would be complementary to SEQ ID NO: 1 and could not possibly comprise at least 30 continuous nucleotides of SEQ ID NO: 1. Further, the currently amended claims are also drawn to 'the complement' for which there is no literal support in the specification or originally

filed claims. The complement of the antisense is the sense. There is no support in the specification or the original claims for 'the complement' of the sequence that hybridizes to the mRNA of tobacco QPRTase having at least 30 continuous sequences of SEQ ID NO: 1 (i.e. a sense fragment), and the specification only recites a sense fragment of at least 15 nucleotides in length on page 11 and does not disclose sense fragments comprising the species of at least 30, 50, 75, 100, 125, 150 or 200 consecutive (i.e. contiguous) nucleotides of SQ ID NO: 1; and thus the claims remain drawn to NEW MATTER. Applicant is invited to point to the page and line number in the specification where support can be found. Absent of such support, Applicant is required to cancel the new matter in the reply to this Office Action.

Claims 1-3, 12-13, 16-19, 26, 31-33, 43-45, 57, 61-62, 95-100 and 103-107 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record set forth in the Official action mailed 4/08/2004 and 7/19/2006. Applicant's arguments filed 8/20/2007 have been considered but are not deemed persuasive.

Applicant asserts that the claims have been amended to recite that the shared structural feature is SEQ ID NO: 1 and the shared activity is hybridizing to the QPRTase mRNA i.e. SEQ ID NO: 1 (response page 8). This is only partly correct, however the claims have been amended to recite that the claimed sequence that hybridizes to QPRTase mRNA has at least 30 consecutive nucleotides of SEQ ID NO: 1. This is not correct. That sequence would have at least

30 nucleotides that are complementary to SEQ ID NO: 1, se page 10 of specification lines 14-28. Moreover, the complement as recited at the end of the claim would not share the activity of hybridizing to SEQ ID NO: 1 because it would be a fragment of SEQ ID NO: 1 and not its complement.

Claims 1-3, 12-13, 16-19, 26, 31-33, 43-45, 57, 61-62, 95-100 and 103-107 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO: 1 encoding SEQ ID NO: 2, tobacco plants transformed with an antisense copy of SEQ ID NO: 1, a method of reducing QPRTase expression in transformed tobacco cells and tobacco plants, and a method of reducing nicotine levels in tobacco plants transformed with an antisense DNA of SEQ ID NO: 1, does not reasonably provide enablement for using any DNA sequence encoding any QPRTase or any portion or segment thereof, or a method of reducing QPRTase expression or nicotine levels in any plant other than a method of reducing QPRTase expression in a tobacco plant transformed with antisense DNA of SEQ ID NO: 1 and transformed tobacco plants therewith. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. This rejection is maintained for the reasons of record set forth in the Official action mailed 4/08/2004 and 7/19/2006. Applicant's arguments filed 8/20/2007 have been considered but are not deemed persuasive.

Applicant asserts under "The breadth of the claims" (response page 12) that the specification provides support for the claimed invention. See arguments supra.

Applicant asserts that the lack of working examples is not required to satisfy the enablement requirement as long as it does not require undue experimentation (response page 13).

In the present case it is not just undue experimentation where one of skill could reasonably expect a successful outcome, but rather it is a case of undue 'trial and error experiemntation' that was well outside the range of even of one of skill in the art. Applicants filed Appendix of 8/20/2007 reciting references directed to sense and antisense fragments are almost all after the effective priority date of 6/12/1997; and that that are before the priority date are not directed to plants and are experiments performed with fragments larger than 200 nucleotides in length.

Applicant's specification provides no articles whatsoever directed to fragments of antisense as small as 30 or 200 nucleotides in length and none discuss sense suppression using fragments. Clearly the state of the art was not developed to an enabling degree and is reflected in Applicant's specification in the complete lack of any working examples using fragments and the lack of adequate references or experimental guidance.

Further, the invention should find support in the specification and not rely upon those of skill in the art. See *In re Fisher,* 166 USPQ 18, 24(CCPA 1970) which teaches "That paragraph (35 USC 112, first) requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." Moreover, Applicant cannot rely upon one of skill in the art given the lack of guidance in the specification and the limited scope of Applicant's disclosure with respect

to the claimed fragments and plants transformed therewith. See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a "mere germ of an idea does not constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

The state-of-the-art is such that one of skill in the art cannot predict whether less than full length gene constructs would predictably retrieve a reduction in gene expression or product expression. Evidence of unpredictability in plants transformed with antisense or sense constructs comprising a fragment of a gene is seen in experiments comparing double stranded cystathione beta-lyase snse-antisense constructs comprising a 1200 bp. Fragment of the full length gene and antisense and sense constructs of the same fragment size. Table 1 on page 764 shows that antisense had no deviation from the wild type phenotype in 23 transformants, and sense constructs had a weak non-lethal effect relative to wild type in 2 of the 13 transformants (Levin J. *et al.* Plant Molecular Biology; 2000, Vol. 44, pp. 759-775; see also abstract and page 766 1st full paragraph). The specification fails to provide guidance for portions or segments of any QPRTase encoding DNA sequence, or which 5' and 3' untranslated regions thereof, that would enable the methods of the claims. Applicant is invited, pursuant to the interview of 7/28/2004, to submit a declaration with data showing evidence of sense and antisense fragments of SEQ ID NO: 1 as small as 30 consecutive nucleotides that reduce nicotine in transformed tobacco.

Based upon Applicant's limited guidance one cannot predict which embodiments would be operable and thus undue trial and error experimentation would be required by one of skill in the art to isolate and test the multitude of non-exemplified DNA fragments and screen a myriad of non-exemplified transformed plants from any species for reduced QPRTase expression and

nicotine content encompassed by the claims.

Given the unpredictability in the art as to which portions or segments of SEQ ID NO: 1 when transformed into tobacco would reduce expression of an endogenous QPRTase and reduce nicotine levels; the breadth of the claims encompassing any fragment as small as 30 consecutive nucleotides of SEQ ID NO: 1 when transformed into tobacco would reduce QPRTase expression or yield reduced levels of nicotine; the lack of guidance in the examples of the specification or in the prior art as to which nucleotide fragments, or portions or segments thereof, would reduce QPRTase expression levels or reduce levels of nicotine in a transformed tobacco; and the undue trial and error experimentation required to practice the claimed invention, the invention is not enabled for the scope set forth in the claims.

All claims are rejected.

The Claims are deemed free of the prior art given the failure of the prior art to teach or suggest DNA sequences encoding a QPRTase and methods of making plant cells and plants transformed therewith wherein the levels of QPRTase or nicotine are reduced.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Russell Kallis Ph.D.
October 17, 2007

RUSSELL P. KALLIS, PH.D.
PRIMARY EXAMINER